Attorney Docket No. 19921/66-CIP (WAA-03-326)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S):	Gerhardt et al.	CONFIRMATION NO.:	9505
SERIAL NO.:	10/723,973	GROUP NO.:	1723
FILING DATE:	November 26, 2003	EXAMINER:	Ernest G. Therkorn
TITLE:	Flow Sensing Apparatus Used to Monitor/Provide Feedback to a Split Flow Pumping System		

Commissioner for Patents
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APPEAL BRIEF

Sir:

This is an appeal from the final rejection of claims 13-17. A Notice of Appeal for this application was received by the United States Patent and Trademark Office on April 12, 2007.

A two-month extension of time up to and including August 12, 2007, for filing an Appeal Brief, is respectfully requested. A petition for the extension of time and appropriate fee are submitted herewith as is the fee set forth in § 41.20(b)(2) for filing the brief. Also submitted herewith are Claims, Evidence and Related Proceedings Appendices.

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(1) **Real party in interest**

The real party in interest in the above-identified patent application is Waters Investments Limited, the assignee of record, which is a subsidiary of Waters Corporation. An assignment perfecting Waters Investments Limited's interest in this application was recorded by the USPTO on June 11, 2007 at reel/frame 019417/0947.

(2) Related appeals and interferences

To the best of the Appellants' knowledge, there are no related appeals or interferences.

(3) Status of claims

Claims 1-12 and 18 are withdrawn, due to a requirement for restriction.

Claims 13-17, as originally filed, are rejected and are the claims on appeal.

(4) Status of amendments

No amendments of the claims have been filed.

(5) Summary of claimed subject matter

As defined by appealed independent claim 13, Appellants' invention relates to a method for measuring nano-scale flow rates of a liquid in a high-pressure liquid chromatography (HPLC) system. Laboratory and production workers utilize HPLC systems to separate liquid-based sample compounds. The separation process supports chemical analyses, drug manufacturing, and other uses.

The inventive method relates to an improvement for HPLC systems that obtain a relatively low liquid flow rate from a relatively high flow-rate pump by splitting the output of the pump. As defined by claim 13, a relatively high flow-rate HPLC pump has its output split into a nano-scale working flow, available to carry a sample, and a higher rate remainder waste flow. See Specification, page 1/lines 17-19.

Specifically, with reference to Figure 3, the claimed method is implemented in an HPLC system that includes an HPLC pump (26), a main flow path (10) leading from the HPLC pump (10), a waste flow path (16), an operating flow path (14), and a flow divider (12) that divides the main flow path (10) into the operating flow path (14) and the waste flow path (16). See Specification, page 10/lines 24-26. The relatively high flow-rate pump (26) has its output split to produce a nano-scale operating flow having a flow rate in a range of about 10 nL/min to about 500 nL/min. See Specification, page 1/lines 14-15. The nano-scale operating flow is supplied to, for example, an HPLC separation column (27). See Specification, page 11/lines 5-6.

The method for measuring nano-scale flow rates, as defined by claim 13, provides an indirectly measured empirical split ratio for the operating flow rate. The method includes:

measuring the main flow rate in the main flow path (10) (using, for example, a main flow sensor (18)); measuring the waste flow rate in the waste flow path (16) (using, for example, a waste flow sensor (20)); subtracting the measured waste flow rate from the main flow rate; and dividing the difference by the main flow rate to determine the empirical split ratio. See claim 13 and Figure 3.

In this manner, and in contrast to prior methods, the claimed invention provides measurement of a nano-scale flow rate in an operating flow path (14) of an HPLC system by measuring flow rates in the main and waste flow paths (10, 16). An empirical (i.e., measured) split ratio of the operating flow rate relative to the main flow rate is obtained in a manner that is insensitive to composition variations of the fluid. See Specification, page 12/lines 2-25. The inventive method supports control of nano-scale flow rates while permitting use of both higher flow-rate pumps and higher flow-rate sensors. See Specification, page 11/lines 25-30.

(6) Grounds of rejection to be reviewed on appeal

1. The first issue presented for appeal is whether appealed claims 13-17 are patentable under 35 U.S.C. §102(b) over either German Patent No. 19,914,358 A1 to Weissgerber et al. or German Patent No. 19,914,358 C2 to Weissgerber et al., with U.S. Patent No. 6,627,075 to Weissgerber et al. serving as a translation of both German patent references.

2. The second issue presented for appeal is whether appealed claims 13-17 are patentable under 35 U.S.C. §103(a) over either German Patent No. 19,914,358 A1 to Weissgerber et al. or German Patent No. 19,914,358 C2 to Weissgerber et al., with U.S. Patent No. 6,627,075 to Weissgerber et al. serving as a translation of both German patent references.

3. The third issue presented for appeal is whether appealed claims 13-17 are patentable under 35 U.S.C. §103(a) over either German Patent No. 19,914,358 A1 to Weissgerber et al. or German Patent No. 19,914,358 C2 to Weissgerber et al. in view of U.S. Patent No. 6,402,946 to Spraul, with U.S. Patent No. 6,627,075 to Weissgerber et al. serving as a translation of both German patent references.

4. The fourth issue presented for appeal is whether appealed claims 13-17 are patentable under 35 U.S.C. §103(a) over either German Patent No. 19,914,358 A1 to Weissgerber et al. or German Patent No. 19,914,358 C2 to Weissgerber et al. in view of European Patent No. 1,248,096 to Zimmermann, with U.S. Patent No. 6,627,075 to Weissgerber et al. serving as a translation of both German patent references.

5. Although Appellants believe that the above-identified issues correspond to all of the pending rejections, Appellants also appeal any other bases for rejection of the pending claims

which were not explicitly stated in the Office action but which may be regarded as still pending.

(7) Argument

Appellants believe that there are no outstanding claim rejections under 35 U.S.C. §112, first or second paragraph. The following argument addresses the issues presented for appeal.

Independent claim 13 and dependent claims 14-17 stand or fall together. Accordingly, Appellants make all arguments with respect to claim 13.

7.1. Claim 13 is patentable under 35 U.S.C. §102(b) over the Weissgerber patent references

Claim 13 is patentable under 35 U.S.C. §102(b) over German Patent No. 19,914,358 A1 to Weissgerber et al. and German Patent No. 19,914,358 C2 to Weissgerber et al., with U.S. Patent No. 6,627,075 to Weissgerber et al. (hereinafter referred to as "Weissgerber '075") serving as a translation of both German patents. This conclusion is supported by the following reasons.

As a preliminary matter, Applicants note that cited German Patent Nos. 19,914,358 A1 and 19,914,358 C2 are different published versions associated with the same German patent application (A1 indicating the unexamined application and C2 indicating the second publication of the issued patent.) The Final Office action, dated December 12, 2006, states that Weissgerber '075 "will serve as a translation of each of" Nos. 19,914,358 A1 and 19,914,358 C2 (Weissgerber '075 claims foreign priority to German Patent No. 19,914,358 and has identical figures to that of the two German Weissgerber references.) Accordingly, all arguments herein are made with reference to Weissgerber '075.

Although Weissgerber '075 and the present invention, as defined by independent claim 13, are superficially related, Weissgerber does not teach all of the features recited by claim

13. Both Weissgerber '075 and the claimed invention relate to chromatography performed at relatively low fluid-flow rates, where a low fluid-flow rate is obtained by splitting a main or total flow of a fluid pump into an operating (i.e., working) flow at the low flow rate and a waste (i.e., excess) flow at a higher flow rate. The claimed invention diverges from Weissgerber '075, however, in how the relatively low flow rate in the operating path is measured. As described in the following, Weissgerber '075 follows a conventional approach that relies on direct measurement of low flow rates in an operating path, while the claimed invention eliminates problems associated with direct measurement of low flow rates by empirically determining a split ratio associated with the operating flow rate through measurement of the higher waste and main flow rates.

Regarding anticipation of independent claim 13, Weissgerber '075 does not disclose indirectly measuring nano-scale flow rates by determining a flow-rate difference between a waste-flow rate, <u>measured in a waste-flow path</u>, and a main-flow rate, <u>measured in a main-flow path</u>, and dividing the flow-rate difference by the main-flow rate <u>to determine an empirical split ratio of an operating-flow rate</u> to the main-flow rate. In contrast, all four devices described by Weissgerber '075 include direct measurement of flow rate in an operating (working) path, in one of three configurations: 1) in an operating path alone (see Weissgerber '075, FIG. 1 and FIG. 2); 2) in an operating path in combination only with measurement of a flow rate in a main path (see Weissgerber '075, FIG. 4); or 3) in an operating path in combination only with measurement of a flow rate in a waste path (see Weissgerber '075, FIG. 3). <u>See</u>, <u>e.g.</u>, Weissgerber '075, col. 2/line 53 (under the section heading "Summary of the Invention," teaching that "in particular…the device has at least one working

sensor.") In no case does Weissgerber '075 teach measurement of flow rate in a waste-flow path in combination with measurement of flow rate in a main-flow path.

The four devices (20, 25, 27, 28) described by Weissgerber '075 include three devices (20, 25, 27) "for preparing very small liquid volume flows" and one device (28) "for calibrating mass flow rate working sensor **40**." See, e.g., Weissgerber '075, col. 6/lines 44-45, col. 8/lines 31-32, and FIGS. 1, 2, 3 and 4. Of the three devices (20, 25, 27) "for preparing very small liquid volume flows", the device (20), as illustrated in FIG. 1, includes only one sensor, a working sensor (40) directly disposed in a working-path conduit (37). The device (25), as illustrated in "the preferred alternative design example of" FIG. 2, includes only one sensor, again, the working sensor (40) directly disposed in the working-path conduit (37). See Weissgerber '075, col. 7/lines 42-43. Last, the device (27), as illustrated in FIG. 3, includes only two sensors, a pressure sensor (67) in the excess-flow path conduit (36) and a pressure sensor (66) in the working-path conduit (37). See, e.g., Weissgerber '075, col. 8/lines 10-12; see, also, Weissgerber '075, col. 7/lines 28-34 (teaching that the "[w]orking sensor **40** can…be arranged at any…suitable point in the path of working flow **35**" (emphasis added.))

The device (28) "for calibrating mass flow rate working sensor **40**", as illustrated in FIG. 4, includes only two sensors: the working sensor (40) in the working-path conduit (37) and a pressure sensor (83) in the total-flow conduit (31). See, e.g., Weissgerber '075, col. 8/lines 37-40 (describing how "[the pressure] sensor **83** monitors the pressure in total flow conduit **31**…[and can] be connected at other suitable points, for example in working path **37**.") Therefore, regarding a total-flow conduit,

Weissgerber '075 at most only suggests measuring pressure in the total-flow conduit to assist calibration of directly measured working flow. For the reasons described above, Weissgerber '075 teaches provision of low-flow rates in a manner that requires direct measurement of the low-flow rate either alone or in combination only with one other measurement: either in the excess path conduit (36) or in the total flow conduit (37).

For the above reasons, claim 13 is not anticipated by Weissgerber '075. Hence, Appellants respectfully submit that claim 13 is patentable under 35 U.S.C. §102(b) over Weissgerber '075. Appellants respectfully request reversal of the rejection of claims 13-17 under 35 U.S.C. §102(b).

7.2. Claim 13 is patentable under 35 U.S.C. §103(a) over the Weissgerber patent references

Claim 13 is patentable under 35 U.S.C. §103(a) over German Patent No. 19,914,358 A1 to Weissgerber et al. and German Patent No. 19,914,358 C2 to Weissgerber et al., with Weissgerber '075 serving as a translation of both German patents (as described in section 7.1, above, all arguments herein are made with reference to Weissgerber '075.) This conclusion is supported by at least four reasons. ***First***, the invention recited by independent claim 13 is not a mere optimization of elements disclosed by Weissgerber '075 because claim 13 recites a combination of elements not disclosed by Weissgerber '075. ***Second***, the invention recited by claim 13 is not a mere rearrangement of elements disclosed by Weissgerber '075 because Weissgerber '075 teaches flow control methods that require direct measurement of a working flow rate. ***Third***, Weissgerber '075's definition of the terms "excess flow", "total flow" and "working flow" does not

render the claimed invention obvious because the undisputed arithmetic relationship between these terms does not disclose the claimed combination of elements. ***Fourth***, the claimed invention provides a solution to the problem of nano-flow rate measurement in split-flow systems in a manner contrary to the conventional approaches taught by Weissgerber '075. These reasons are described in more detail below.

As a preliminary matter, as described in Section 7.1, Weissgerber '075 does not teach measuring nano-scale flow rates by determining a flow-rate difference between a waste-flow rate, measured in a waste-flow path, and a main-flow rate, measured in a main-flow path, and dividing the flow-rate difference by the main-flow rate to determine an empirical split ratio of an operating-flow rate to the main-flow rate, all as recited by independent claim 13. Indeed, as described in Section 7.1, Weissgerber '075 teaches solutions to the problem of working flow control that require direct measurement of a working flow.

First, the claimed invention does not merely optimize elements disclosed by Weissgerber '075 because the invention, as recited by claim 13, includes a combination of elements not disclosed by Weissgerber '075. The Final Office Action asserts that "if a difference exists between the claims and [Weissgerber '075], it would reside in optimizing the elements of [Weissgerber '075]. It would have been obvious to optimize the elements of [Weissgerber '075] to enhance measurements." See Final Office Action, page 2/line 7 from bottom to page 3/line 2. This bare statement, however, is unsupported by the contents of Weissgerber '075. See, e.g., *KSR v. Teleflex*, No. 04-1350, 550 U.S. __ (2007), Slip at 14 ("'[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead there must be

some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness'" (quoting *In re Kahn*, 441 F. 3d 977, 988 (CA Fed. 2006).))

The claimed invention does not optimize elements of the Weissgerber '075 devices (20, 25, 27, 28), which, as described in Section 7.1, require direct measurement of an operating flow path, because claim 13 recites a combination of elements that include no requirement of direct measurement of the operating flow path. As recited by claim 13, the empirical ratio associated with the operating flow is obtained from direct measurements of the <u>main</u> flow and the <u>waste</u> flow; the claimed invention does not "optimize" elements disclosed by Weissgerber '075, where the claimed invention eliminates the requirement of an element that is essential in the Weissgerber '075 devices (20, 25, 27, 28); the claimed invention includes different elements, not optimized elements, in comparison to Weissgerber '075.

Second, Weissgerber '075 does not render obvious a rearrangement of elements taught by Weissgerber '075 to include measurement of a total flow in combination with measurement of a waste flow to obtain a split ratio associated with a working flow because all that Weissgerber '075 teaches requires direct measurement of the working flow rate. <u>See</u>, <u>e.g.</u>, MPEP (Eighth Edition, Rev'd August 2006) § 2144.04,VI,C (quoting *Ex parte Chicago Rawhide Mfg. Co.*, 223 USPQ 351 as stating that "[t]he mere fact that a worker in the art could rearrange the parts of the reference device to meet the terms of the claims on appeal is not by itself sufficient to support a finding of obviousness. The prior art must provide a motivation or reason for the worker in the art, without the benefit of appellant's specification, to make the necessary changes in the reference device.")

Weissgerber '075 not only provides no reason for a rearrangement of flow measurement elements to eliminate a need for direct measurement of the working flow rate; Weissgerber '075 teaches away from such a rearrangement because Weissgerber '075 is entirely directed to mitigating problems associated with direct measurement of working flow rate with solutions that always include direct measurement of the working flow rate. See *KSR*, 550 U.S. __ (2007), Slip at 12 (reiterating the "principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvous") (citing *United States v. Adams*, 383 U.S. 39, 51-52 (1966)); see, also, *KSR*, 550 U.S. __ (2007), Slip at 17 (stating that "[a] factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning" and reiterating the "warning against a 'temptation to read into the prior art the teachings of the invention in issue.'" (quoting *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 36 (1966))).

Regarding split-flow systems, Weissgerber '075 utilizes an approach that is conventional at least to the extent that Weissgerber '075 relies on direct measurement of the low-flow working path. Moreover, to deal with the known problem of calibration of measurements made in a low-flow path, Weissgerber '075 proposes a method of calibration of the direct measurements of flow rate in the low-flow working path. See Weissgerber '075, col. 8/lines 37-40, and FIG. 4 (regarding the device (28) "for calibrating mass flow rate working sensor **40**" in the working-path conduit (37).)

Thus, Weissgerber '075 presents solutions that rely on conventional system configurations, in contrast to the claimed

invention, which eliminates a need for such solutions. As noted in the Specification, the claimed invention is not merely a rearrangement or optimization of elements disclosed by Weissgerber '075; the claimed invention provides a distinct improvement over everything taught and suggested by Weissgerber '075. Indeed, a need for calibration is obviated by the invention, as claimed. See Specification, page 12/lines 22-25 ("in contrast to heretofore known systems for measuring flow rates in a range from about 10 nL/min. to about 1000 mL/min. which must typically be calibrated for particular liquid composition, the flow sensing method of the present invention is insensitive to the composition of the fluid being measured.")

Third, Weissgerber '075 merely defines the terms "excess flow", "total flow" and "working flow" without providing any disclosure regarding indirect measurement of a working flow path because all of Weissgerber '075 entails direct measurement of working flow. The Final Office Action mischaracterizes the disclosure of Weissgerber '075 regarding measurement of working flow; the Final Office Action asserts that Weissgerber '075's statement that "[t]he excess flow is the difference between the total flow 32…and the working flow 35" (see Weissgerber '075, column 6, lines 56-58) teaches that "one of the two subdivided flow paths can be calculated from the total flow minus the other subdivided flow path." See Final Office Action page 4/second paragraph. The Weissgerber '075 statement at most, however, merely expresses the arithmetic relationship of the terms "excess flow", "total flow" and "working flow". The arithmetic relationship of these terms, i.e., total flow = working flow + excess flow, is not in dispute; the statement in Weissgerber '075 reflects the inherent relationship of flow components in a device (20) that includes a total flow (32) that is split only into a

working flow (35) and an excess flow (34). See, e.g., Weissgerber, Figure 1.

Moreover, the statement of Weissgerber '075 reinforces Weissgerber '075's teaching that the working flow (35) is a directly measured quantity. See Weissgerber '075, column 6/lines 56-58 (implying that working flow and total flow are measured by stating that "[t]he excess flow is the difference between the total flow **32**…and the working flow **35**.") Indeed, the Weissgerber '075 statement arguably is worded in this manner because all that Weissgerber '075 contemplates includes, at a minimum and in contrast to the claimed invention, a sensor disposed in the working flow path for direct measurement of the working flow.

Fourth, the invention, as defined by claim 13, provides a solution to problems encountered in both conventional systems and the devices described in Weissgerber '075; as described above, these systems and devices control nano-scale flow rates in split-flow systems by measuring flow directly in a working/operating flow path (i.e., the split path that carries the nano-scale flow rate.)

Thus Weissgerber '075 does no more than reinforce the conventional thinking that one directly measures nano-scale flow rates in a working path, and attempts to mitigate associated calibration problems. The claimed invention provides an improved implementation of nano-scale flow rate HPLC by eliminating the requirement of direct measurement in the nano-scale flow-rate working path. In contrast, Weissgerber '075 provides a solution to the problem of measuring low flow rates that continues to rely on direct observations in the working path. See Weissgerber '075, column 7/lines 7-9 (with reference to FIG. 1, stating that "[w]orking sensor **40** can however also be arranged at any other

suitable point in the path of working flow **35**" (emphasis added)); see, also, Weissgerber '075, column 10/lines 17-28 (concluding the Detailed Description by mentioning that "other design variants are possible," but the variants still utilize direct observation of a working flow path.)

For the above reasons, Appellants respectfully submit that claim 13 is patentable under 35 U.S.C. §103(a) over Weissgerber '075. Appellants respectfully request reversal of the rejection of claims 13-17 under 35 U.S.C. §103(a).

7.3. Claim 13 is patentable under 35 U.S.C. §103(a) over the Weissgerber patent references in view of Spraul

Claim 13 is patentable under 35 U.S.C. §103(a) over either German Patent No. 19,914,358 A1 to Weissgerber et al. or German Patent No. 19,914,358 C2 to Weissgerber et al. (with Weissgerber '075 serving as a translation of both German patents,) in view of U.S. Patent No. 6,402,946 to Spraul. This conclusion is supported by the reasons described below. As described in Section 7.1, arguments with respect to the Weissgerber family of patent documents are made with reference to Weissgerber '075.

Regarding Weissgerber '075 alone, as described above in Section 7.2, independent claim 13 is nonobvious because Weissgerber '075 does not teach that the empirical split ratio associated with a nano-scale operating-flow rate is obtained by determining a flow-rate difference between a waste-flow rate, measured in a waste-flow path, and a main-flow rate, measured in a main-flow path, and dividing this flow-rate difference by the main-flow rate.

Independent claim 13 is also nonobvious in view of the combination of Weissgerber '075 and Spraul because Spraul adds nothing to the deficiencies of Weissgerber '075 with regard to

the features recited by claim 13. Moreover, in contrast to the claimed invention, Spraul teaches that a sample flow is split according to a chosen split ratio, and not that that the split ratio is empirically determined. Indeed, Spraul provides no disclosure regarding measurement of any flow rate. See Spraul, column 8/lines 3-6 (stating that "[t]he splitter **40** can be fixed or free adjustable [and] must only meet the requirements to split the flow…in a suited ratio and to provide an exact flow after the split.")

Rather than teaching any method of measuring any flow rate, Spraul teaches a switching method to provide portions of separated samples for analyses by various detectors (20, 26, 22). See, e.g., Spraul, column 12/lines 22-32. Spraul merely describes splitting and switching the output of a chromatography separation to provide separate sample flows to the inputs of a liquid-chromatography (LC) detector (20) and to a mass-spectrometry (MS) detector (26); the sample flow to the LC detector (20) may also proceed to a nuclear magnetic resonance (NMR) detector (22). See, e.g., Spraul, Fig. 1; see, also, Spraul, column 2/lines 10-21 (describing the problem of splitting flows "in order to connect [an] LC-NMR system with [an] MS.")

In contrast to the features recited by claim 13, Spraul describes preferred values of a selected split ratio. See Spraul, column 2/lines 10-21 (stating that "[t]he split ratio [is] varied from case to case between 50:1 and 20:1" with the larger flow to the NMR detector and the lower flow to the MS detector); and see Spraul, column 8/lines 8-10 (stating that "[t]he split ratio [of capillaries feeding two detectors] is preferably chosen as 20:1, wherein the major part of the flow is fed [to the NMR] and the minor part [to the MS].")

To provide different flow rates for chromatographic separation of samples and subsequent analyses of parked separated samples, Spraul teaches the combined use of a chromatography pump and a dilutor pump (86); the dilutor pump (86) provides a lower flow rate than the chromatography pump. See, e.g., Spraul, Fig. 8 and column 4/lines 24-27 ("[b]y means of the dilutor pump, a flow rate for feeding the parked peak into the second destination detector unit can be chosen different from the flow rate generated by the chromatography pump"); see, also, Spraul, column 10/lines 45-50 ("[b]y switching the first valve means **38** now into the operating position shown in **FIG. 7**, the peak parked in the second delay line **84** can be fed to the MS detector **26** by connecting the dilutor pump **86** to the third capillary line **36.** The peak now can be fed with a very low flow rate to the MS detector"); and see Spraul, column 12/lines 41-45 ("the dilutor pump **86** starts to pump in a very low speed.") Thus, Spraul teaches methods to produce different flow rates of separated samples, but does not teach methods to measure nano-scale flow rates nor to determine an empirical split ratio of an operating flow.

For the above reasons, Appellants respectfully submit that claim 13 is patentable under 35 U.S.C. §103(a) over Weissgerber '075 in view of Spraul. Appellants respectfully request reversal of the rejection of claims 13-17 under 35 U.S.C. §103(a).

7.4. Claim 13 is patentable under 35 U.S.C. §103(a) over the Weissgerber patent references in view of Zimmerman

Claim 13 is patentable under 35 U.S.C. §103(a) over either German Patent No. 19,914,358 A1 to Weissgerber et al. or German Patent No. 19,914,358 C2 to Weissgerber et al., with Weissgerber '075 serving as a translation of both German patents, in view of European Patent No. 1,248,096 to Zimmermann. This conclusion is

supported by the reasons described below. As described in Section 7.1, arguments with respect to the Weissgerber family of patent documents are made with reference to Weissgerber '075.

In view of Weissgerber '075 alone, independent claim 13 is nonobvious for the reasons described in Section 7.2. In particular, Weissgerber '075 does not render obvious a method for measuring nano-scale flow rates in which an empirical ratio associated with an operating flow rate that is obtained by determining a flow-rate difference between a waste flow rate, measured in a waste-flow path, and a main flow rate, measured in a main-flow path, and dividing this flow-rate difference by the main flow rate.

Independent claim 13 is nonobvious in view of the combination of Weissgerber '075 and Zimmerman because Zimmerman, like Weissgerber '075, teaches that the flow in a split working or operating path is directly measured with a sensor placed in the working or operating path. See Zimmerman, column 3/lines 4-6 ("[i]t is effective here if the working sensors are designed as flow sensors directly measuring the fluid flow"); see, also, Zimmerman, column 3/lines 19-20 ("[a]t least one of the working sensors is assigned advantageously to each of the divided fluid flows.")

Zimmerman, in contrast to the features recited by claim 13, teaches that a single flow can be split into two or more partial-flow working paths, and that a sensor is placed in every split working path. See Zimmerman, column 2/lines 10-13. In particular, Zimmerman describes two flow dividers (20, 60) (illustrated, respectively, in Figures 1 and 2) that each include sensors in every split path; the dividers (20, 60) "hav[e] a reduced back pressure sensitivity, enabling the splitting ratio

[between the split paths] to be kept constant independently of the physical properties of the fluid and/or the fluctuations in pressure." See Zimmerman, column 3/line 57 to column 4/line 1. Zimmerman teaches that the flow in two or more split working paths is directly measured in each path so that the ratio of the flows in at least two of the working paths can be kept constant. See Zimmerman, column 4/lines 2-4 ("by means of at least a number of working sensors corresponding to the number of divided fluid flows…the ratio between at least two of the [divided] fluid flows remains substantially constant."); and see Zimmerman, Figure 2, and column 5/lines 12-14 (the divider [60] splits in the flow into four partial flows [71, 72, 73, 74] and "[e]ach of the four splitter branches 75, 76, 77, 78 comprises a working sensor 81, 82, 83, 84 designed as flow sensor.")

In contrast to the limitations recited by claim 13, Zimmerman does not teach measuring the total flow. Also, in contrast to claim 13, Zimmerman does not teach an empirically determined split ratio for a working flow that is determined, in part, by measuring a waste-flow rate in a waste-flow path and measuring a main-flow rate in a main-flow path; instead, Zimmerman merely teaches the direct measurement of working flow in every working flow path and use of a splitter ratio between the directly observed working flow paths. See Zimmerman, column 4/lines 41-45 ("the computer unit 55 serves to calculate the splitter ratio, that is, the ratio of the volume rates of fluid flow 31 and fluid flow 30 [i.e., two split working paths] from the measurement signals detected by working sensors 41 and 42.")

For the above reasons, Appellants respectfully submit that claim 13 is patentable under 35 U.S.C. §103(a) over Weissgerber '075 in view of Zimmerman. Appellants respectfully request

reversal of the rejection of claims 13-17 under 35 U.S.C. §103(a).

7.5 The claimed invention is patentable under any other possible bases for rejection

Appellants believe that the foregoing arguments address each of the pending rejections of the pending claims. In particular, the present Brief addresses each of the rejections made final. Accordingly, Appellants submit that the present application meets all requirements for patentability.

Conclusion

For the reasons given above, Appellants respectfully request that the rejections be reversed and the application be allowed with claims 13-17 as presented in the Appendix attached hereto.

Respectfully submitted,

Date: July 20, 2007

/Jamie H. Rose/
Jamie H. Rose
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Claims Appendix

13. A method for measuring nano-scale flow rates of a liquid in a high pressure liquid chromatography (HPLC) system comprising: measuring a main flow rate in a main flow path between an HPLC pump and a flow-divider; dividing said main flow path into an operating flow path and a waste flow path according to a split ratio of said flow-divider; measuring a waste flow rate in said waste flow path; subtracting said waste flow rate from said main flow rate to determine a flow rate difference; dividing said flow rate difference by said main flow rate to determine an empirical split ratio.

14. The method according to claim 13 wherein said empirical split ratio is independent of varying liquid composition.

15. The method according to claim 13 further comprising: adjusting the liquid flow rate in said operating flow path in response to said empirical split ratio.

16. The method according to claim 15 further comprising disposing a variable restrictor in said waste flow path and wherein said liquid flow rate in said operating flow path is adjusted by changing the permeability of said variable restrictor.

17. The method according to claim 15 wherein said step of adjusting involves adjusting liquid flow in said operating flow path by changing the output flow rate of said HPLC pump.

Evidence Appendix

NONE.

Related Proceedings Appendix

NONE.